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A Functional Analysis of the Early Development of Self-Injurious Behavior:

Incorporating Gene-Environment Interactions

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Abstract

The analysis of the early development of self-injurious behavior has to date reflected the wider distinction between ‘nature’ and ‘nurture’. Despite the status of genetic factors as risk markers for the later development of self-injurious behavior, a model that accounts for their influence on early behavior-environment relations is lacking. In the current paper we argue that the investigation of gene-environment interactions (GxE) and other forms of gene-environment interplay could potentially enhance current approaches to the study of self-injury. A conceptual model of the early development of self-injurious behavior based explicitly on such relations is presented. The model is consistent with the basic tenets of functional analysis. Implications for research and the assessment, treatment and prevention of self-injurious behavior are discussed.

A Functional Analysis of the Early Development of Self-Injurious Behavior:
Incorporating Gene-Environment Interactions

Self-injurious behavior is one of the most challenging forms of behavior displayed by individuals with intellectual and developmental disabilities. Self-injurious behavior refers to behaviors, such as head-hitting or scratching, that people direct towards themselves and which results in tissue damage (Tate & Baroff, 1966). Such behaviors have a pervasive impact on the quality of life of the individual, exerting not only negative physical but also negative social consequences (Robertson et al., 2004), and therefore represent a significant barrier to child development. Given its devastating impact, intervening before self-injurious behavior becomes an established part of the child's repertoire holds many apparent benefits. The advantages of early intervention for children with autism have been well documented (McEachin, Smith, & Lovaas, 1993), however with only a few exceptions (e.g., Wacker et al., 1998), the same cannot be said of early intervention for self-injurious behavior. In part, this may be due to a limited understanding of the factors that lead to the genesis of self-injurious behavior (Symons, Sperry, Holditch-Davis, & Miles, 2003).

Existing conceptual models of the early development of self-injurious behavior have focused almost exclusively on the role of environmental factors (Guess & Carr, 1991; Oliver, 1993). Guess and Carr (1991), for example, argued that initially automatically reinforced stereotypical behaviors are shaped into increasingly severe topographies of self-injurious behavior, as they begin to contact socially and non-socially mediated contingencies of reinforcement. Whilst a growing literature exists to support

this model (e.g., Richman & Lindauer, 2005) the influence of biological and genetic factors on early behavior-environment relations remains poorly understood.

Gene-environment interactions (GxE) have been investigated and shown to exert powerful effects in the development of several physical and mental health disorders (see Rutter, Moffitt, & Caspi, 2006 for a review). The GxE approach has developed from the observations that many behavioral disorders are causally influenced by environmental pathogens but with wide individual differences in response to such pathogens (Caspi & Moffitt, 2006). In these fields it is now recognised that the traditional view of there being additive, and non-interactive effects between genes and environment is somewhat misplaced. However the distinction has to some extent remained intact in the investigation of self-injurious behavior. The investigation of GxE is one component of a more general approach towards the study of gene-environment interplay; an approach which also comprises examination of the effects of environment on gene expression, the effects of environment on genetic heritability and correlations between genes and environment (Rutter et al., 2006). In what follows the consequences of maintaining the false dichotomy between 'nature' and 'nurture' are discussed, before an expanded model of the early development and maintenance of self-injurious behavior is proposed. The model presents a functional analysis of self-injurious behavior based explicitly upon GxE and other forms of gene-environment interplay.

Genes and self-injurious behavior

Self-injurious behavior in certain cases is clearly influenced by genetic sources of variability. Evidence suggests that certain forms of self-injurious behavior may constitute part of the behavioral phenotype of a number of genetic syndromes. Gene to

behavior associations of varying specificity have been repeatedly demonstrated across a number of syndromes; including Lesch-Nyhan syndrome (Nyhan, 1972), fragile X syndrome (Symons, Clark, Hatton, Skinner, & Bailey, 2003), and Smith-Magenis syndrome (Finucane, Dirrigl, & Simon, 2001).

Few would subscribe to the view that genes ‘cause’ such behaviors. There is considerable within-syndrome variability in the extent to which individuals with a given syndrome go on to develop behaviors considered ‘phenotypic’ (Hodapp & Dykens, 2001). Environmental factors have been shown to contribute to such variability (Hessl et al., 2001). Even in cases where strong gene-behavior associations do exist it does not necessarily follow that these occur independent of environmental influence. For example, even at the molecular level the environment has been shown to alter gene expression (Restivo et al., 2005). Gene-behavior associations reflect not only the direct effect of genes but also the effects of environment and, where present, the effects of gene-environment interplay. It is not necessarily the case, therefore, that a strong gene-behavior association indicates the absence of environmental influence. Despite the apparent ubiquity of gene-environment interplay, however, most behavioral phenotype research has failed to go beyond the demonstration of simple gene-behavior associations (Hodapp & Dykens, 2001).

The continued neglect of environmental influences in behavioral phenotype research may limit our understanding of the development of self-injurious behavior and paradoxically the role that genes play in this process. As Moffitt, Caspi and Rutter (2005) state:

Ignoring nurture may have handicapped the field's ability to understand nature
(p.478).

The functional effects of genes upon behavioral development remain poorly understood. There is a need for behavioral phenotype researchers to go beyond gene-behavior association and to begin to incorporate GxE relations and other forms of gene-environment interplay into the study of self-injurious behavior.

Environment and self-injurious behavior

Others have focused exclusively on the environmental determinants of self-injurious behavior. Functional analysis is the hallmark of the applied behavior analytic approach to the assessment and treatment of self-injurious behavior (Hanley, Iwata, & McCord, 2003). Over the past decade, investigators have begun to incorporate an individual's biological functioning into the analysis of such behaviors (Langthorne, McGill, & O'Reilly, 2007). This has had a profound impact on the assessment and treatment of self-injurious behavior displayed by people with intellectual and developmental disabilities.

However, the influence of genetic and other biological variables has not yet been integrated with models of the early development of self-injurious behavior. Despite the status of genetic syndromes as significant 'risk markers' for the later development of self-injurious behavior (McClintock, Hall, & Oliver, 2003), a conceptual model that accounts for their influence on early behavior-environment relations is lacking. Secondly, the focus of behavior analysis on behavioral function has led to a neglect of form. As has been repeatedly demonstrated there are highly specific relationships between certain

genetic syndromes and particular topographies of self-injurious behavior which current 'operant' models say little about.

The omission of genetic influences from functional analysis stems from a 'misunderstanding' of the relations between biological and behavioral events and an assumption that such factors are private, inaccessible and in some cases hypothetical (Thompson, 2007). Such an omission is particularly striking given that central to the operant model, from which the functional analysis of self-injurious behavior has itself evolved, is the phylogenic and ontogenic selection of behavior (Skinner, 1966). Behavior analysis as a philosophy and a science is contextual (Morris, 1988), and the occurrence of any response can only be understood in regard to the historical and current context (both genetic and environmental) in which that act is embedded. Paradoxically, despite the prominence Skinner gave to genetic influences, their analysis has remained largely outside the realm of applied behavior analysis.

GxE Interactions and the Early Development of Self-Injurious Behavior

A GxE approach is based on the assertion that environmental 'pathogens' cause behavioral disorders and genes influence susceptibility to these 'pathogens' (Caspi & Moffitt, 2006). Several studies have recently demonstrated that the effects of exposure to an environmental 'pathogen' may be conditional on a person's genotype. In the first such study, Caspi et al. (2002) demonstrated that a functional polymorphism in the gene encoding the neurotransmitter-metabolizing enzyme monoamineoxidase A (MAOA) served to moderate the effects of child maltreatment on the later development of anti-social behavior. Specifically, individuals who had low levels of MAOA and experienced childhood maltreatment were more likely to develop anti-social behaviors than were

individuals with a high-activity MAOA genotype exposed to the same ‘pathogen’.

Similar GxE relations have been shown to influence the development of psychosis in adolescent cannabis users (Caspi et al., 2005), and the development of ADHD symptoms (Brookes et al., 2006).

Genes do not code for specific behaviors, rather the effects of genes upon behavior-environment relations are by virtue of their effects on the organism as a whole developmental system (Johnston & Edwards, 2002). This system comprises of bidirectional relations between environmental, behavioral, physiological, neural and genetic sources of variability (Gottlieb, 2003). The role of DNA is to specify the production of mRNA, which then in turn determines the production of the polypeptides that form proteins. It is these proteins that act upon the development of the individual. This process is epigenetic and is itself influenced by environmental factors. The role of genes therefore is to influence the development of the organism as a whole (across neural, physiological, and behavioral pathways); it is this whole organism which then interacts with the environment.

The model proposed in the current paper is based on the thesis that in some cases genes influence susceptibility to known environmental ‘pathogens’ for the development of self-injurious behavior. To date researchers have typically examined either genetic or environmental factors whilst overlooking the interaction between the two. A conceptual framework is needed to examine the influence of such interactions as they apply to self-injurious behavior. We provide an operant analysis of GxE and other forms of gene-environment interplay and suggest that genes may alter basic behavior-environment

relations by virtue of their effect on the developmental system. The implications of such a model for the study, treatment and prevention of self-injurious behavior are discussed.

A Functional Analysis of the Early Development of Self-Injurious Behavior

How do genes influence the development of the organism in a way that has specific effects on subsequent behavior-environment relations? It has been postulated that genes may influence behavior-environment relations in a number of ways (e.g., Moore, 2002; Skinner, 1966). Conceptually, at least, such factors may alter the developmental system in a way that influences; (1) the stream of 'uncommitted' behavior from which an operant response evolves, that is they may contribute to initial behavioral variation. (2) the sensitivity of the individual to changes in environmental stimulation, that is they may either facilitate or inhibit the discrimination of stimulus events and (3) the value of certain environmental consequences that serve to reinforce or punish behavior, that is they may establish or abolish the 'motivation' for the consequences that maintain self-injurious behavior. These effects are likely to be achieved by the influence of genes on neurobiological and physiological pathways.

Figure 1 provides a schematic representation of a model of the early development of self-injurious behavior based on the relations discussed above. Many of the environmental elements to this model have been comprehensively addressed in previous accounts of the development of self-injurious behavior (Guess & Carr, 1991; Oliver, 1993). The influence of genetic factors and the role of certain other biological factors (such as health conditions), however, have to date escaped systematic appraisal. The model consists of seven stages, which for schematic purposes are presented in a linear

fashion; this is not to imply that the model necessarily follows a linear path of causation or that all stages are necessary for the development of self-injurious behavior.

In stage 1, genetic events alter the development of the individual in a way that influences the emission of 'uncommitted' topographies of behavior from which an operant response evolves. The analysis of general movements may hold particular clues for our understanding of the later development of self-injurious behavior (Symons, Sperry et al., 2003). Thus, genes contribute to initial behavioral variation, albeit pre and post-natal environmental factors may also influence this. In stage 2 it is recognized that some forms of uncommitted behavior are more likely to elicit a social response than are others and this waxes and wanes over time as the environment itself adapts to the behavior of the child. This stage is critical in the evolution from uncommitted behavior to self-injurious behavior. In stage 3 genetic events (in addition to pre- and post-natal environmental factors) alter individual development in such a way that determines the discrimination of stimuli. Thus genetic factors may in part determine the discrimination of certain stimulus events and thereby alter the likelihood with which certain contingencies are formed. In stage 4 self-injurious behavior contacts socially and non-socially mediated contingencies of reinforcement to become operant. Both genetic (stage 5) and environmental (stage 6) events establish these contingencies as effective forms of reinforcement and evoke self-injurious behavior by functioning as motivating operations. Finally in stage 7, the process of habituation shapes increasingly severe topographies of child behavior.

Stage 1. Genetic events supply uncommitted topographies of behavior

A response must be first emitted ‘for some other reason’ before it can become operant (Skinner, 1966). It seems that genetic factors may play an important role in helping to determine the initial stream of ‘uncommitted’ behavior, out of which increasingly complex operant responses evolve. In some cases such uncommitted behaviors may be of initial survival value to the organism, for example as in the rooting reflex of a newborn baby, and are the building blocks out of which complex behavior, such as *manding* for food, are shaped. Evidence from animal models suggests that genetic manipulations influence the emission of motor activity (such as the degree of environmental ‘exploration’) which facilitates or inhibits the subsequent development of behavior-environment relations (McKerchar, Zarcone, & Fowler, 2005). Both genetic and environmental factors alter the developmental system in such a way as to influence the initial uncommitted behaviors that an individual emits.

Newborn infants display prominent and complex movement patterns, termed general movements, which follow a predictable developmental course (Einspieler & Prechtl, 2005). Whilst general movements may be influenced by environmental factors, such as pre- or postnatal injury or exposure to toxins, there is a large genetic contribution to such movements. General movements have been observed both in vitro and post-natally and are thought to antecede the development of ‘voluntary’ (or rather operant) behavior. Thelen (1979) noted the importance of early rhythmic motor behavior for motor development in typically-developing infants. Qualitative differences in general movements have been shown to differentiate between low-risk and high-risk pre-term infants (Prechtl, 1990). In addition early patterns of general movements predict later problems in child development, such as cerebral palsy (Cioni et al., 1997).

It has been suggested that the analysis of general movements may hold some 'clues' for the later development of self-injurious behavior (Symons, Sperry et al., 2003). However to date there have been no attempts to integrate this with existing conceptual accounts of self-injurious behavior. The initial occurrence of general movements may represent the building blocks out of which self-injurious behavior evolves. There are some parallels here with the motor control hypothesis of stereotypical and self-injurious behavior. For example, evidence suggests that the motor control of individuals who display stereotypy differs from controls (Bodfish, Parker, Lewis, Sprague, & Newell, 2001). It has been suggested that the root of such differences in motor control may lie in a dopamine deficiency in basal ganglia functioning (Turner & Lewis, 2002). Work with deer mice has shown that the prevention or attenuation of stereotypical behaviors through environmental enrichment occurs only for mice who show enrichment-related differences in cortical-basal ganglia circuitry (Lewis, Tanimura, Lee, & Bodfish, 2007).

Rett syndrome and Down syndrome are two of the few genetic syndromes for which general movements have been empirically investigated (Einspieler, Kerr, & Prechtl, 2005; Mazzone, Mugno, & Mazzone, 2004). In a retrospective study, Einspieler et al. (2005) found that the quality of general movements in 26 infants, who had been diagnosed with Rett syndrome, was considerably impaired. By 4-months of age all of the infants had impaired 'fidgety' general movements, which were topographically different from those observed in infants with acquired brain lesions. Four of the infants with Rett syndrome were observed to have tremulous movements in the arms. The chromosomal basis of Rett syndrome lies in a mutation of the MeCP2 gene, a mutation which has pervasive effects on brain development. The disorder is associated with structural

reductions in the basal ganglia and the decreased production of dopamine transporters, leading to the altered pattern of motor development associated with the syndrome (Schroeder et al., 2001). The effect of the MeCP2 gene mutation on brain development is likely to give rise to a pattern of impaired general movements that quickly contact contingencies of reinforcement. Indeed the stereotypical and self-injurious behaviors associated with Rett syndrome have been shown to be influenced by both automatic and socially mediated consequences (e.g., Oliver, Murphy, Crayton, & Corbett, 1993).

Such relations may hold relevance for the later development of self-injurious behavior in other genetic syndromes. Lesch-Nyhan syndrome, for example, is characterized by a particular movement disorder (Nyhan, 1972). Early movements characteristic of this syndrome include involuntary spasmodic, wild, and violent movements of the face, shoulders and hips, which are present at 8-12 months of age. This precedes the development of self-injurious behavior, which has a typical onset at between 2 and 3 ¹/₂ years of age. The movement disorder associated with Lesch-Nyhan syndrome has been associated with the impaired functioning of the dopaminergic system (Wong et al., 1996). The concentration of dopamine transporters does not, however, differentiate between individuals with Lesch-Nyhan syndrome who have both the movement disorder and self-injurious behavior and those with only the movement disorder (Harris et al., 1999), suggesting that dopamine depletion is not sufficient to account for the development of self-injurious behavior (Schroeder et al., 2001). There may be a GxE relationship underpinning this observation. For example, the HPRT deficiency results in changes in brain structure and function which leads to the emission of certain 'uncommitted' behaviors which are likely to expose a child with Lesch-Nyhan syndrome

to environmental 'pathogens' for self-injurious behavior. Hypothetically, a child with Lesch-Nyhan syndrome may accidentally bang their head as a result of reflex extension, part of the movement disorder associated with the syndrome, before that response comes under social control (Hall, Oliver, & Murphy, 2001). In the absence of differential social reinforcement (the environmental pathogen) SIB would not be expected to develop.

Smith-Magenis syndrome is a genetic syndrome associated with severe self-injurious behavior, which includes the removal of finger- and toenails. Empirical evidence on the origin and function of this behavior is scarce. However, Finucane et al (2001) speculate that its origin may lie in the altered neuropathy associated with the syndrome. Clinical signs of peripheral neuropathy have been reported in approximately 75% of SMS patients (Greenberg et al., 1996). Specifically, it has been hypothesized that abnormal sensations in peripheral nerves lead the child to pull at his or her toenails. Such 'uncommitted' behavior is likely to quickly be selected by its environmental consequences (e.g., social contact from parents) and acquire operant status. Again, the hypothesis here is that the interstitial deletion of chromosome 17p11.2 in Smith-Magenis syndrome leads to damage of the peripheral nervous system, resulting in behavior which exposes the child to known 'pathogens' for the development of self-injurious behavior.

It has been argued that genes (in addition to pre- and post-natal environmental factors) influence the emission of uncommitted behaviors by acting on the individual at a neurobiological and physiological level. Specific examples of how and why this may occur have been provided for three different syndromes. It would seem that the assessment of general movements in children with genetic syndromes associated with self-injurious behavior as well as the neurobiology underpinning such movements may be

an important avenue for future research. This pattern of development, in which general movements precede the development of self-injurious behavior, complements existing models and empirical evidence on the development of self-injurious behavior.

Stage 2. The environment is more sensitive to certain topographies of child behavior

Evidence suggests that one way in which genetic factors interact with the environment may be to indirectly influence the extent to which an individual is exposed to environmental ‘pathogens’ for a behavioral disorder (Rutter et al., 2006). Several studies have demonstrated the impact of such gene-environment correlations on the development of a range of disorders (Ge et al., 1996). In the context of the current discussion ‘uncommitted’ child behavior, such as the reflex extension associated with Lesch-Nyhan syndrome, is likely to evoke a particular response from parents and caregivers. Once evoked these adult responses are likely to lead to the child being exposed to known environmental ‘pathogens’.

It is the differential responsiveness of the environment to certain topographies of behavior that is so critical for the environmental selection of operant behavior (Bijou, 1966). To the extent that certain forms of child behavior serve as aversive stimuli their onset may function as motivating operations (Laraway, Snyckerski, Michael, & Poling, 2003) for the removal or attenuation of that behavior. In the context of the current model parents and caregivers may be more likely to respond to particular ‘uncommitted’ behaviors (such as the wild and violent movements associated with Lesch-Nyhan syndrome) than they are to others. This is likely to be essential in the evolution from uncommitted behavior to self-injurious behavior. Parental responses that are successful in removing such behaviors are then more likely to occur in the future (Oliver, 1993). A

broad range of contextual variables, such as parental stress (Hastings, 2002), may influence the degree to which parents are differentially responsive to atypical child motor movements.

There is a body of evidence to suggest that (a) particular topographies of child behavior function as an aversive stimulus for parents and caregivers (e.g., Hastings, 2002), (b) child behavior functions as a *motivating operation* for adult responses to that behavior (e.g., Taylor & Carr, 1992) and (c) that the responses of adults serve to reinforce self-injurious behavior (e.g., Richman & Lindauer, 2005). Thus adult responses to self-injurious behavior are themselves shaped by the behavior of the child. The role of genes in this process is to influence the likelihood of the child's exposure to such 'risky' environments.

Stage 3. Genetic events determine the sensitivity of the nervous system to changes in environmental stimulation

Genetic events may help determine the sensitivity of the individual to various forms of environmental stimulation (Moore, 2002; Skinner, 1966). The ability to discriminate stimulus events is critical for the development of behavior-environment relations. Someone who is congenitally blind is unlikely to be sensitive to a change in visual stimulation; conversely an individual with 20/20 vision is likely to be particularly sensitive to such a change. The result of such genetically (and environmentally) determined changes may be to enhance, or conversely diminish, an individual's susceptibility to the discrimination of certain stimulus events.

Some genetic influences may *restrict* the sensitivity of the individual to a stimulus event, whereas other genetic influences may *enhance* sensitivity to particular stimulus

events. This is likely to be achieved by the influence of genes on the development of the individual at a neurobiological and physiological level. Reiss et al (2004) provided evidence that the impaired visual-spatial abilities and enhanced face processing and emotionality associated with Williams syndrome had specific neuroanatomical correlates. Magnetic resonance imaging scans showed that participants with Williams syndrome had reduced thalamic and occipital lobe grey matter volumes and reduced grey matter density in subcortical and cortical regions comprising the visual-spatial system, in comparison to controls. The Williams syndrome group also showed increases in volume and grey matter density in areas known to be involved in emotion and face processing. Thus, a specific genetic event (interstitial deletion of chromosome 7) was shown to be related to neuroanatomical changes, which themselves are related to the ability to discriminate specific stimuli. Clearly environmental factors may also contribute to such individual differences in brain development. Given that the ability to discriminate a stimulus change is a necessary pre-requisite for the establishment of behavior-environment contingencies then such differences may hold an important function for the early development of self-injurious behavior. It is surprising therefore, that such factors have not, to date, received attention in existing models of the early development of self-injurious behavior.

A number of genetic syndromes may be associated with the altered ability to discriminate certain stimulus events. For example, individuals with fragile X syndrome appear to be particularly sensitive to changes in social and sensory stimulation (Kau et al., 2004), perhaps potentiating the establishment of contingencies between their behavior and social/sensory consequences. Hyperacusis (sensitivity to sound) is present in as many

as 95% of individuals with Williams syndrome (Klein, Armstrong, Greer, & Brown, 1990). Genetic events may also reduce sensitivity to certain stimulus events. Cornelia de Lange syndrome, for example, is associated with minimal responsiveness to sound or pain (Johnson, Ekman, Freisen, Nyhan, & Shear, 1976). A reduced sensitivity to pain may prevent the establishment of a contingency between self-injurious behavior and its painful automatic consequences.

Whilst the degree to which autism can be regarded to be a genetic disorder is of some controversy, what has been repeatedly demonstrated is that many individuals diagnosed with autism show an altered ability to discriminate certain stimuli. For example, autism is associated with an enhanced response and slower habituation rate to the repeated presentation of a tactile stimulus (Baranek & Berkson, 1994). Likewise, autism is associated with an enhanced auditory discrimination (O'Riordan & Passetti, 2006) whereas certain visual stimuli are less likely to be discriminated (Bertone, Mottron, Jelenic, & Faubert, 2003). Although the source of such variability (i.e., genetic or environmental) is of some debate, it does seem possible that the altered ability to discriminate changes in stimulation may influence the later development of behavior-environment relations.

In sum, both genetic and environmental events may influence the extent to which changes in environmental stimulation are discriminated; a necessary pre-requisite for the development of an operant response, such as self-injurious behavior. Such relations may alter the individual's responsiveness to known environmental 'pathogens' for the development of self-injurious behavior, and thereby constitutes a potential GxE.

Stage 4. Child behavior meets contingencies of reinforcement & forms part of a response class

A primary aim of functional analysis is to identify those consequences that maintain self-injurious behavior. It is beyond the scope of this paper to provide a review of this area; however, three areas of research are of particular relevance.

Firstly, research spanning three decades has shown that self-injurious behavior displayed by people with intellectual and developmental disabilities may be evoked and maintained by its environmental antecedents and consequences (Hanley et al., 2003). Secondly, it has been demonstrated that self-injurious behavior displayed by individuals with genetic syndromes may be influenced by environmental events. For example, Hall, Oliver and Murphy (2001) demonstrated that patterns of self-injurious behavior displayed by three boys with Lesch-Nyhan syndrome were consistent with a positive reinforcement hypothesis. Such evidence demonstrates that self-injurious behaviors displayed by individuals with genetic syndromes may be influenced by environmental contingencies. Thirdly, empirical evidence shows that social and non-social reinforcement is critical in the early development of self-injurious behavior (e.g., Richman & Lindauer, 2005). In sum, a body of evidence exists to suggest environmental factors are critical in the development and maintenance of self-injurious behavior, even when that behavior is specifically associated with genetic syndromes. Such factors represent known ‘pathogens’ for the development of self-injurious behavior and it may be that genetic variables influence the extent to which an individual exposed to such environmental events goes on to develop self-injurious behavior.

Stage 5. Genetic events function as motivating operations

The variables of which behavior is a function comprise of more than the contingency between response and consequence. One important contextual variable is the motivating operation. Motivating operations refer to stimuli, stimulus conditions or operations that alter the value of consequences as reinforcers and the probability of behaviors being evoked that have historically been associated with those consequences (Laraway et al., 2003). The analysis of such events has been typically restricted to environmental events, such as the deprivation of attention or onset of aversive stimuli (McGill, 1999). However, genetic events may also alter the value of those consequences that maintain self-injurious behavior (Kennedy, Caruso, & Thompson, 2001). Evidence from animal models exists to suggest that specific genetic manipulations may exert motivational effects on the reinforcing value of appetitive reinforcers (Hayward & Low, 2007; Thomsen & Caine, 2006).

Although the evidence-base is small and somewhat limited, individuals with certain genetic syndromes may be more likely to display behaviors that serve specific functions. A number of single-case studies have shown that stereotypical and self-injurious behaviors associated with Rett syndrome may be especially likely to be maintained by either escape from aversive stimuli and/or automatic reinforcement (Iwata, Pace, Willis, Gamache, & Hyman, 1986; Oliver et al., 1993; Wales, Charman, & Mount, 2004). Likewise, Prader-Willi syndrome appears to be related to tangible-maintained challenging behaviors (Clarke, Boer, & Webb, 1995; Kennedy et al., 2001). Finally, studies which have relied on indirect functional assessment or antecedent manipulations suggest that fragile X syndrome may be specifically associated with challenging behavior, including self-injurious behavior, that is maintained by the contingent removal

of aversive stimuli (Hall, DeBernadis, & Reiss, 2006; Symons, Clark et al., 2003). A postal survey study conducted by Symons, Clark et al. (2003) found that parents reported 87% of participants with fragile X syndrome displayed such behaviors in response to routine changes, and 65% in response to task demands. In contrast only 3% of participants were reported to display such behaviors to access attention. Hall et al (2006) recently reported a relatively large-scale study, involving some 114 children with fragile X syndrome in which patterns of responding were directly observed during antecedent manipulation of environmental conditions. Challenging behaviors were more likely to occur in conditions characterized by high social or performance demands.

Genes do not directly influence behavior, and the relations discussed are likely to be influenced by the impact of genetic events upon the developmental system as a whole (Gottlieb, 2003). Some genetic syndromes are associated with certain physiological conditions, and it may be that such conditions play an important role in establishing the 'motivation' for self-injurious behavior. For example, sleep disturbance is reported to be present in 65-100% cases of Smith-Magenis syndrome (Greenberg et al., 1996). In cases, in which sleep disturbance associated with Smith-Magenis syndrome is shown to influence self-injurious behavior, then treatment of the sleep disturbance may be one possible early intervention. (De Leersnyder et al., 2007). Such relations may be important in regards to the function served by self-injurious behavior associated with other genetic syndromes. For example, fragile X syndrome is thought to be associated with the abnormal activation of the limbic-hypothalamic-pituitary-adrenal (L-HPA) axis, a system primarily involved in the human stress response, the activation of which leads to the secretion of cortisol (Hessl et al., 2002). Hessl et al (2002) found higher cortisol levels to

be positively associated with parental reports of the severity of problem behaviors displayed by males and females with fragile X syndrome. It may be that the absence of the FMR1 protein leads to changes in the development of the L-HPA axis which enduringly heightens the probability of negatively reinforced behavior. In regards to Prader-Willi syndrome, Holland, Whittington and Hinton (2003) have speculated that the genetic abnormality underlying Prader-Willi syndrome leads to the impaired functioning of the hypothalamic pathways and the absence of metabolic and psychological changes that normally follow food intake. People with Prader-Willi syndrome have been shown to have an abnormally high blood level of the hormone ghrelin which serves to enduringly heighten the reinforcing value of food (Del Parigi et al., 2002).

In sum, self-injurious behavior is unlikely to develop unless there exists some 'motivation' for the consequences that are responsible for its maintenance. It seems that genetic factors may in some cases be the source of such 'motivation'. Evidence for this remains at a preliminary stage and few studies have met the standards of an experimental functional analysis (Hanley et al., 2003). Further studies based on the group comparison of individual data sets from individuals with different genetic syndromes are required. In cases in which genetically based motivating operations are present it would seem likely that these effects are enduring, rather than momentary. In such cases, there may be a particular 'sensitivity' to small fluctuations in environmental levels of the reinforcer that maintains the behavior. This is likely to form a GxE that potentiates known 'pathogens' for the development of self-injurious behavior. Such influences are likely to have important implications for the early assessment and intervention of self-injurious

behavior and are not currently integrated with any existing conceptual model of the early development of self-injurious behavior.

Stage 6. Ontogenic factors (physiological, neurobiological and environmental) function as motivating operations

The environments in which many people with intellectual and developmental disabilities spend a large proportion of their time are replete with characteristics that establish the ‘motivation’ for self-injurious behavior. Such behaviors may be more likely to develop in environments that are austere or barren of stimulation, lacking in attention and access to preferred items and activities, high in aversive stimuli and social control (e.g., Berg et al., 2000; O'Reilly, 1999). Certain neurobiological factors, such as the direct and side-effects of psychotropic drugs (Northup et al., 1999) and certain physiological conditions such as sleep deprivation and allergy symptoms (Kennedy & Meyer, 1996) may also function as motivating operations. Thus, a range of ontogenic variables are likely to establish the effectiveness of the consequences that maintain self-injurious behavior.

Stage 7: Increasingly severe topographies of self-injurious behavior are shaped via a process of habituation

The final stage of our model functions as a feedback mechanism to account for the selection of increasingly severe topographies of self-injurious behavior over time. Adult responses *habituate* to the repeated presentation of aversive stimuli, such as early forms of self-injurious behavior. A number of empirical studies have shown that the repeated presentation of a reinforcer leads to habituation, which may bring about changes in operant responding (Murphy, McSweeney, Smith, & McComas, 2003).

Habituation to reinforcement may serve as a motivating operation for parent behavior by exerting an abolishing effect on the effectiveness of the removal of child self-injurious behavior (Oliver, 1993). This habituation process leads to the extinction of the contingency between self-injurious behavior and its environmental consequences. This is likely to influence child behavior by leading to an increase in the rate, intensity or variability of self-injurious behavior. In the current context, increases in the intensity, rate, or variety of early self-injurious behavior may serve to *re-establish* the removal of child behavior as an effective type of reinforcement and *evoke* adult responses that have led to this in the past. This final stage accounts for how initially uncommitted behaviors are transformed into increasingly severe topographies of self-injurious behavior.

Implications for the Assessment, Treatment, and Prevention of Self-Injurious Behavior

In the current paper we have extended existing models of the genesis of self-injurious behavior by incorporating GxE relations and other forms of gene-environment interplay. We argue that exposure to environmental ‘pathogens’ is necessary for the development of self-injury. We have provided an account of why certain genetic syndromes are a risk marker for the development of self-injury (McClintock et al., 2003), suggesting that genes may alter susceptibility to such ‘pathogens’. Specifically genes may influence the development of self-injurious behavior by acting on the individual in a way that; (1) provides uncommitted behavior out of which self-injurious behavior later develops, (2) influences the discrimination of certain stimulus events (3) enduringly alters the value of certain consequences that function as reinforcers. However, self-injury would not be expected to develop in the absence of exposure to environmental ‘pathogens’.

Such a conceptual expansion may hold important implications for the assessment, treatment and prevention of such behaviors. One of the benefits of this analysis is that it may enable the development of environmental modifications that provide a better fit to the needs of the individual. For example, knowledge of GxE relations and other forms of gene-environment interplay may facilitate environmental changes that serve to prevent or remediate self-injurious behavior. In addition, adopting a more integrated perspective may have consequences for the study of self-injurious behavior. Some of the applied and research implications of this expanded model shall therefore be discussed in greater detail.

Stage 1 suggests that uncommitted behaviors are the building blocks out of which self-injurious behavior evolves. The comprehensive assessment of uncommitted behavior may also hold implications for attempts at prevention. If a particular genetic syndrome is associated with general movements that are likely to evoke a caregiver response then a prevention-based approach, targeting parental responses to such behaviors may hold some promise in reducing the adventitious reinforcement of such behavior. In addition, the absence of certain general movements could spur the development of a prosthetic environment, which facilitates the development of alternative behavioral sets.

As suggested in stage 3 of the model, genetic influences may also determine the discrimination of certain stimulus events. This may have a number of implications for the early prevention of self-injurious behavior. Environmental or neurobiological modifications could be introduced to reduce the sensitivity of the individual to particular stimulus events. For example, earplugs could be offered to children with Williams syndrome to reduce the sensitivity of the individual to changes in noise levels (O'Reilly,

Lacey, & Lancioni, 2000). In other cases environmental or neurobiological interventions may be required to improve the individual's ability to form certain behavior-environment contingencies. For example, the use of the opiate antagonist *naltrexone* may enhance the development of a contingency between self-injurious behavior and its automatic aversive consequences (Sandman, Barron, & Colman, 1990). This would have all the elements of a punishment procedure albeit with the aim of establishing a typical rather than atypical experience of pain.

In stage 5 we suggest that genetic events may function as enduring motivating operations for self-injurious behavior. This holds an array of implications for the treatment and prevention of self-injury. Early functionally equivalent responses could be reinforced using consequences for which 'susceptibility' is thought to exist at a time before a clear function for self-injurious behavior is apparent. Such an approach would seem to be particularly necessary given the reported difficulty in ascribing function to self-injurious behavior displayed by very young children (Kurtz et al., 2003). This area has been subject to only a small amount of research and a systematic approach is now required that develops our knowledge of the value- and behavior-altering influences of certain genetic influences. Further investigation of the pathways underlying such relations may provide an additional point of intervention.

The enthusiasm surrounding gene-environment interplay has been dampened by legitimate concerns surrounding the pragmatic difficulties of conducting such research. In order for this conceptualisation to influence the behavior of researchers these concerns need to be addressed. Moffitt et al (2005) have proposed a seven-step strategy for the identification of GxE interactions and, in comparison to other fields, investigators of self-

injurious behavior are in a relative position of strength to begin the search for GxE and other forms of gene-environment interplay. First, it is well established that there are certain syndromes associated with the heightened prevalence of self-injurious behavior, but that there exists considerable within-syndrome variability. Second, there is clear empirical evidence of the causal status of environmental ‘pathogens’ for the development of self-injurious behavior. Third, we have established methods of measuring the influence of such ‘pathogens’ over time. Fourth, behavioral phenotype research has led to the identification of several candidate ‘susceptibility’ genes for self-injurious behavior. In short we know enough about environmental and genetic influences to begin to construct specific and testable hypotheses about relations between genes and the environment and their role in the development of self-injurious behavior.

How can such interactions begin to be examined? Large scale, longitudinal, prospective cohort studies in which the individual acts as his or her own control are the most powerful means of testing specific GxE hypotheses (Moffitt et al., 2005). Studying self-injurious behavior as it develops already forms an important research agenda (e.g., Richman & Lindauer, 2005); future studies could examine whether individuals with specific genetic syndromes differ in terms of their susceptibility to the known environmental ‘pathogens’ measured in such studies. Existing developmental studies could also be retrospectively examined to see whether differences exist in regards to the developmental pattern of individuals with certain genetic syndromes in comparison to others.

Specific hypotheses based on some of the postulations made in the current paper would seem to warrant further examination. For example, the assessment of early

movements displayed by infants with certain genetic syndromes, such as Lesch-Nyhan syndrome, may provide a fruitful source of research. The extent to which such differences predict the actual development of self-injurious behavior, and whether the presence of environmental ‘pathogens’ are necessary for this to occur, would form an important research agenda. Further study of the potential motivative effects of genes upon behavior-environment relations also seems to be an important research question. Group control studies that followed the methodology used in current behavioral phenotype research, except with an emphasis on function rather than form, may constitute one means of testing such hypotheses. In addition further investigation of the neurobiological and physiological pathways that underpin such relations would seem to be of considerable importance (Turner & Lewis, 2002). A focus on the proximal effects of genes on the developing organism (i.e., the endophenotype) may hold important implications for our understanding of gene-environment interplay (Gottesman & Gould, 2003). Animal models, which allow for a greater degree of experimental control, may provide an important tool in this quest, indeed empirical examples of gene-brain-behavior-environment relations already exist in the experimental literature (e.g., Hayward & Low, 2007).

In general, the analysis of GxE relations and other forms of gene-environment interplay has the potential to contribute to a more comprehensive approach to the understanding of self-injurious behavior. Indeed if genetic effects operate through influencing susceptibility to environmental ‘pathogens’ then a reduction in such ‘pathogens’ will decrease the likelihood of the development of self-injurious behavior. At a molar level this could contribute to effective environmental manipulations that prevent

the development of self-injurious behavior when an otherwise high risk for their development exists. Such an approach would be analogous to the prevention of the deleterious effects of phenylketonuria through dietary control.

Conclusion

The development of any operant response is embedded in a context of gene-environment interplay. This context is likely to involve mutual interactions between variables at the genetic, neurological, physiological, behavioral and environmental level (Johnston & Edwards, 2002). Such relations have not been integrated with existing models of the early development of self-injurious behavior. In the current paper we have provided a conceptual model of self-injurious behavior, one that remains compatible with the basic tenets of functional analysis. GxE relations and other forms of gene-environment interplay may be critically important, particularly when self-injurious behavior is correlated with genetic syndromes. The evidence reviewed suggests that genetic influences are an important source of variability; one that applied behavior analysis may need to begin to come to terms with. The experimental tactic of demonstrating functional relationships between dependent and independent variables provides one means of uncovering the nature of this interaction.

References

- Baranek, G. T., & Berkson, G. (1994). Tactile Defensiveness in Children with Developmental-Disabilities - Responsiveness and Habituation. *Journal of Autism and Developmental Disorders*, 24(4), 457-471.
- Berg, W. K., Peck, S., Wacker, D. P., Harding, J., McComas, J., Richman, D., et al. (2000). The effects of pre-session exposure to attention on the results of assessments of attention as a reinforcer. *Journal of Applied Behavior Analysis*, 33(4), 463-477.
- Bertone, A., Mottron, L., Jelenic, P., & Faubert, J. (2003). Motion perception in autism: a "complex" issue. *Journal of Cognitive Neuroscience*, 15(2), 218-225.
- Bijou, S. W. (1966). A functional analysis of retarded development. In N. Ellis (Ed.), *International review of research in mental retardation* (Vol. 1, pp. 1-19). New York: Academic Press.
- Bodfish, J. W., Parker, D. E., Lewis, M. H., Sprague, R. L., & Newell, K. M. (2001). Stereotypy and motor control: Differences in the postural stability dynamics of persons with stereotyped and dyskinetic movement disorders. *American Journal on Mental Retardation*, 106(2), 123-134.
- Brookes, K. J., Mill, J., Guindalini, C., Curran, S., Xu, X. H., Knight, J., et al. (2006). A common haplotype of the dopamine transporter gene associated with attention-deficit/hyperactivity disorder and interacting with maternal use of alcohol during pregnancy. *Archives of General Psychiatry*, 63(1), 74-81.
- Caspi, A., McClay, J., Moffitt, T. E., Mill, J., Marin, J., & Craig, I. W. (2002). Role of genotype in the cycle of violence in maltreated children. *Science*, 297, 851-854.

- Caspi, A., & Moffitt, T. E. (2006). Gene-environment interactions in psychiatry: joining forces with neuroscience. *Nature Reviews Neuroscience*, 7, 583-590.
- Caspi, A., Moffitt, T. E., Cannon, M., McClay, J., Murray, R., Harrington, H., et al. (2005). Moderation of the effect of adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the COMT gene: Longitudinal evidence of a gene X environment interaction. *Biological Psychiatry*, 57, 1117-1127.
- Cioni, G., Ferrari, F., Einspieler, C., Paolicelli, P. B., Barbani, M. T., & Prechtel, H. F. R. (1997). Comparison between observation of spontaneous movements and neurologic examination in preterm infants. *Journal of Pediatrics*, 130(5), 704-711.
- Clarke, D. J., Boer, H., & Webb, T. (1995). Genetic and behavioural aspects of Prader-Willi syndrome. *Mental Handicap Research*, 8, 38-53.
- De Leersnyder, H., Bresson, J. L., de Blois, M. C., Souberbielle, J. C., Mogenet, A., Delhotal-Landes, B., et al. (2007). β_1 -adrenergic antagonists and melatonin reset the clock and reset sleep in a circadian disorder, Smith-Magenis syndrome. *Journal of Medical Genetics*, 74-78.
- Del Parigi, A., Tschopo, M., Heiman, M. L., Slalbe, A. D., Vozarova, B., Sell, S. M., et al. (2002). High circulating ghrelin: A potential cause for hyperphagia and obesity in Prader-Willi syndrome. *Journal of Clinical Endocrinology and Metabolism*, 87, 5461-5464.

- Einspieler, C., Kerr, A. M., & Prechtl, H. F. R. (2005). Abnormal general movements in girls with Rett disorder: The first four months of life. *Brain & Development, 27*, S8-S13.
- Einspieler, C., & Prechtl, H. F. R. (2005). Prechtl's assessment of general movements: A diagnostic tool for the functional assessment of the young nervous system. *Mental Retardation and Developmental Disabilities Research Reviews, 11*(1), 61-67.
- Finucane, B., Dirrigl, K. H., & Simon, E. W. (2001). Characterization of self-injurious behaviors in children and adults with Smith-Magenis syndrome. *American Journal on Mental Retardation, 106*(1), 52-58.
- Ge, X., Cogner, R. D., Cadoret, R. J., Neiderhiser, J. M., Yates, W., Troughton, E., et al. (1996). Developmental interface between nature and nurture: A mutual influence model of child antisocial behavior and parent behaviors. *Developmental Psychology, 32*(4), 574-589.
- Gottesman, I. I., & Gould, T. D. (2003). The endophenotype concept in psychiatry: Etymology and strategic intentions. *American Journal of Psychiatry, 160*(4), 636-645.
- Gottlieb, G. (2003). On making behavioral genetics truly developmental. *Human Development, 46*, 337-355.
- Greenberg, F., Lewis, R. A., Potocki, L., Glaze, D., Parke, J., Killian, J., et al. (1996). Multi-disciplinary clinical study of Smith-Magenis syndrome (deletion-17p11.2). *American Journal of Medical Genetics, 62*(3), 247-254.

- Guess, D., & Carr, E. G. (1991). Emergence and maintenance of stereotypy and self-injury. *American Journal on Mental Retardation*, 96(3), 299-319.
- Hall, S., DeBernadis, M., & Reiss, A. (2006). Social escape behaviors in children with fragile X syndrome. *Journal of Autism and Developmental Disorders*, 36(7), 935-947.
- Hall, S., Oliver, C., & Murphy, G. (2001). Self-injurious behaviour in young children with Lesch-Nyhan syndrome. *Developmental Medicine & Child Neurology*, 43, 745-749.
- Hanley, G. P., Iwata, B. A., & McCord, B. E. (2003). Functional analysis of problem behavior a review. *Journal of Applied Behavior Analysis*, 36(2), 147-185.
- Harris, J. C., Wong, D. F., Jinnah, H. A., Schretlen, D., Yokoi, F., Stephane, M., et al. (1999). *Dopamine Transporter Binding of WIN 35,428 Correlates with HPRT Level and Extent of Movement Disorder But Not With Self-Injurious Behavior* Paper presented at the Annual Meeting (No. 855.9), Miami, FL.
- Hastings, R. P. (2002). Parental stress and behaviour problems of children with developmental disability. *Journal of Intellectual & Developmental Disability*, 27(3), 149-160.
- Hayward, M. D., & Low, M. J. (2007). The contribution of endogenous opioids to food reward is dependent on sex and background strain. *Neuroscience*, 144(1), 17-25.
- Hessl, D., Dyer-Friedman, J., Glaser, B., Wisbeck, J., Barajas, R. G., Taylor, A., et al. (2001). The influence of environmental and genetic factors on behavior

- problems and autistic symptoms in boys and girls with fragile X syndrome. *Pediatrics*, *108*(5), 88-97.
- Hessl, D., Glaser, B., Dyer-Friedman, J., Blasey, C., Hastie, T., Gunnar, M., et al. (2002). Cortisol and behavior in fragile X syndrome. *Psychoneuroendocrinology*, *27*, 855-872.
- Hodapp, R. M., & Dykens, E. M. (2001). Strengthening behavioral research on genetic mental retardation syndromes. *American Journal on Mental Retardation*, *106*(1), 4-15.
- Holland, A., Whittington, J., & Hinton, E. (2003). The paradox of Prader-Willi syndrome: a genetic model of starvation. *The Lancet*, *362*, 989-991.
- Iwata, B. A., Pace, G. M., Willis, K. D., Gamache, T. B., & Hyman, S. L. (1986). Operant studies of self-injurious hand biting in the Rett syndrome. *American Journal of Medical Genetics*, *24*, 157-166.
- Johnson, H. G., Ekman, P., Freisen, W., Nyhan, W. L., & Shear, C. (1976). A behavioral phenotype in the de Lange syndrome. *Pediatric research*, *10*, 843-850.
- Johnston, T. D., & Edwards, L. (2002). Genes, interactions, and the development of behavior. *Psychological Review*, *109*, 26-34.
- Kau, A. S., Tierney, E., Bukelis, I., Stump, M. H., Kates, W. R., Trescher, W. H., et al. (2004). Social behavior profile in young males with fragile X syndrome: characteristics and specificity. *American Journal of Medical Genetics*, *126*(1), 9-17.

- Kennedy, C. H., Caruso, M., & Thompson, T. (2001). Experimental analyses of gene-brain-behavior relations: Some notes on their application. *Journal of Applied Behavior Analysis, 34*(4), 539-549.
- Kennedy, C. H., & Meyer, K. A. (1996). Sleep deprivation, allergy symptoms, and negatively reinforced problem behavior. *Journal of Applied Behavior Analysis, 29*(1), 133-135.
- Klein, A. J., Armstrong, B. L., Greer, M. K., & Brown, F. R. (1990). Hyperacusis and otitis-media in individuals with williams syndrome. *Journal of Speech and Hearing Disorders, 55*(2), 339-344.
- Kurtz, P. E., Chin, M. D., Huetee, J. M., Tarbox, R. S. F., O'Connor, J. T., Paclawskyj, T. R., et al. (2003). Functional analysis and treatment of self-injurious behavior in young children: a summary of 30 cases. *Journal of Applied Behavior Analysis, 36*(2), 205-219.
- Langthorne, P. D., McGill, P., & O'Reilly, M. F. (2007). Incorporating motivation into the functional analysis of challenging behavior: On the interactive and integrative potential of the motivating operation. *Behavior Modification, 31*(4), 466-487.
- Laraway, S., Snyckerski, S., Michael, J., & Poling, A. (2003). Motivating operations and some terms to describe them: Some further refinements. *Journal of Applied Behavior Analysis, 36*(3), 407-414.
- Lewis, M. H., Tanimura, Y., Lee, L. W., & Bodfish, J. W. (2007). Animal models of restricted repetitive behavior in autism. *Behavioural Brain Research, 176*(1), 66-74.

- Mazzone, L., Mugno, D., & Mazzone, D. (2004). The general movements in children with Down syndrome. *Early Human Development, 79*(2), 119-130.
- McClintock, K., Hall, S., & Oliver, C. (2003). Risk markers associated with challenging behaviours in people with intellectual disabilities: a meta analytic study. *Journal of Intellectual Disability Research, 47*(6), 405-416.
- McEachin, J. J., Smith, T., & Lovaas, O. I. (1993). Long-term outcome for children with autism who received early intensive behavioral treatment. *American Journal on Mental Retardation, 97*(4), 359-372.
- McKerchar, T. L., Zarcone, T. J., & Fowler, S. C. (2005). Differential acquisition of lever pressing in inbred and outbred mice: Comparison of one-lever and two-lever procedures and correlation with differences in locomotor activity. *Journal of the Experimental Analysis of Behavior, 84*(3), 339-356.
- Moffitt, T. E., Caspi, A., & Rutter, M. (2005). Strategy for investigating interactions between measured genes and measured environments. *Archives of General Psychiatry, 62*, 473-481.
- Moore, J. (2002). Some thoughts on the relation between behavior analysis and behavioral neuroscience. *The Psychological Record, 52*, 261-279.
- Morris, E. K. (1988). Contextualism: The world view of behavior analysis. *Journal of Experimental Child Psychology, 46*, 289-323.
- Murphy, E. S., McSweeney, F. K., Smith, R. G., & McComas, J. J. (2003). Dynamic changes in reinforcer effectiveness: Theoretical, methodological, and practical implications for applied research. *Journal of Applied Behavior Analysis, 36*(4), 421-438.

- Northup, J., Fusilier, I., Swanson, V., Huete, J., Bruce, T., Freeland, J., et al. (1999). Further analysis of the separate and interactive effects of methylphenidate and common classroom contingencies. *Journal of Applied Behavior Analysis*, 32(1), 35-50.
- Nyhan, W. L. (1972). Clinical features of the Lesch-Nyhan syndrome. *Archives of Internal Medicine*, 130, 186-192.
- O'Reilly, M. F. (1999). Effects of pre-session attention on the frequency of attention-maintained behavior. *Journal of Applied Behavior Analysis*, 32(3), 371-374.
- O'Reilly, M. F., Lacey, C., & Lancioni, G. E. (2000). Assessment of the influence of background noise on escape-maintained behavior in a child with Williams syndrome. *Journal of Applied Behavior Analysis*(4), 511-514.
- O'Riordan, M. A., & Passeti, F. (2006). Discrimination in autism within different sensory modalities. *Journal of Autism and Developmental Disorders*, 36(5), 665-675.
- Oliver, C. (1993). Self-injurious behavior- from response to strategy. In C. Kiernan (Ed.), *Research to Practice? Implication of Research on the Challenging Behavior of People with Learning Disabilities* (pp. 135-188). Clevedon: British Institute of Learning Disabilities.
- Oliver, C., Murphy, G. H., Crayton, L., & Corbett, J. (1993). Self-injurious-behavior in Rett syndrome - Interactions between features of Rett syndrome and operant-conditioning. *Journal of Autism and Developmental Disorders*, 23(1), 91-109.

- Prechtl, H. F. R. (1990). Qualitative changes of spontaneous movements in fetus and preterm infant are a marker of neurological dysfunction. *Early Human Development, 23*(3), 151-158.
- Reiss, A. L., Eckert, M. A., Rose, F. E., Karchemskiy, A., Kesler, S., Chang, M., et al. (2004). An experiment of nature: Brain anatomy parallels cognition and behavior in Williams syndrome. *Journal of Neuroscience, 24*(21), 5009-5015.
- Restivo, L., Ferrari, F., Passino, E., Sgobio, C., Bock, J., Oostra, B. A., et al. (2005). Enriched environment promotes behavioral and morphological recovery in a mouse model for the fragile X syndrome. *Proceedings of the National Academy of Sciences of the United States of America 102*(32), 11557-11562.
- Richman, D. M., & Lindauer, S. E. (2005). Longitudinal assessment of stereotypic, proto-injurious, and self-injurious behavior exhibited by young children with developmental delays. *American Journal on Mental Retardation, 110*(6), 439-450.
- Rutter, M., Moffitt, T. E., & Caspi, A. (2006). Gene-environment interplay and psychopathology: multiple varieties but real effects. *Child Psychology and Psychiatry, 47*(3), 226-261.
- Sandman, C. A., Barron, J. L., & Colman, H. (1990). An orally-administered opiate blocker, naltrexone, attenuates self-injurious-behavior. *American Journal on Mental Retardation, 95*(1), 93-102.
- Schroeder, S. R., Oster-Granite, M. L., Berkson, G., Bodfish, J. W., Breese, G. R., Cataldo, M. F., et al. (2001). Self-injurious behavior: Gene-brain-behavior relationships. *Mental Retardation and Developmental Disabilities, 7*, 3-12.

- Skinner, B. F. (1966). The phylogeny and ontogeny of behavior. *Science, 153*, 1205-1213.
- Symons, F. J., Clark, R. D., Hatton, D. D., Skinner, M., & Bailey, D. B. (2003). Self-injurious behavior in young boys with fragile X syndrome. *American Journal of Medical Genetics, 118A*, 115-121.
- Symons, F. J., Sperry, L., Holditch-Davis, D., & Miles, M. S. (2003). Early and self-injurious behavior in young children born at-risk: a preliminary analysis. *Developmental Medicine and Child Neurology, 45*(12), 844-845.
- Tate, B. G., & Baroff, G. S. (1966). Aversive control of self-injurious behavior in a psychotic boy. *Behavior Research and Therapy, 4*, 281-287.
- Thelen, E. (1979). Rhythmic stereotypies in normal human infants. *Animal Behaviour, 27*(699-715).
- Thomsen, M., & Caine, S. B. (2006). Cocaine self-administration under fixed and progressive ratio schedules of reinforcement: comparison of C57BL/6J, 129X1/SvJ, and 129S6/SvEvTac inbred mice. *Psychopharmacology, 184*(2), 145-154.
- Turner, C. A., & Lewis, M. H. (2002). Dopaminergic mechanisms in self-injurious behavior and related disorders. In S. Schroeder, M. Oster-Granite & T. Thompson (Eds.), *Self-injurious Behavior: Gene-Brain-Behavior Relationships* (pp. 165-180). Washington DC: APA.
- Wacker, D. P., Berg, W. K., Harding, J. W., Derby, K. M., Asmus, J. M., & Healy, A. (1998). Evaluation and long-term treatment of aberrant behavior displayed by

young children with developmental disabilities. *Developmental and Behavioral Pediatrics, 19*, 260-266.

Wales, L., Charman, T., & Mount, R. H. (2004). An analogue assessment of repetitive hand behaviours in girls and young women with Rett syndrome. *Journal of Intellectual Disability Research, 48*(7), 672-678.

Wong, D. F., Harris, J. C., Naidu, S., Yokoi, F., Marengo, S., Dannals, R. F., et al. (1996). Dopamine transporters are markedly reduced in Lesch-Nyhan disease in vivo. *Proceedings of the National Academy of Sciences of the United States of America, 93*(11), 5539-5543.

Author Note

The paper contributed towards the first author's doctoral dissertation and was supported by a grant from the *Economic and Social Research Council (ESRC)*, UK. The authors would like to thank the Editor and Reviewers for their comments which were a source of great help in the development of this paper. Correspondence concerning this article should be addressed to Paul Langthorne, Tizard Centre, University of Kent, CT2 7LZ, UK. E-mail: P.Langthorne@kent.ac.uk.

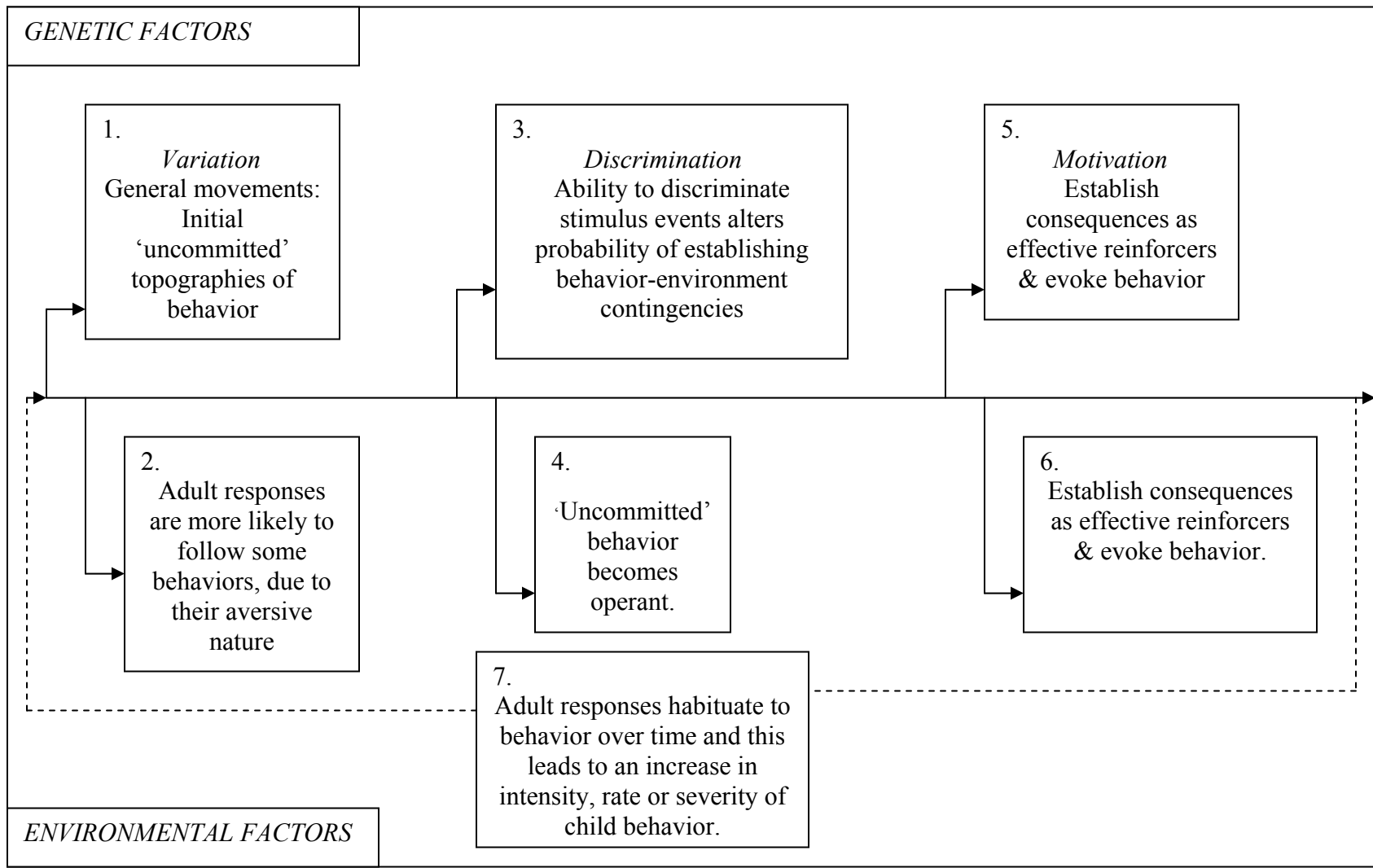


Figure 1: A Model of the Early Development of Self-Injurious Behavior